

Substitute Sequence Listing

<110> VERMEIJ, Paul

<120> Hybrid toxins comprising shiga or shiga-like toxin subunits fused to escherichia coli heat labile enterotoxin subunits and vaccines thereof

<130> I-2003.006 US

<150> PCT/EP2004/051522

<151> 2004-07-16

<150> EP 03077266.9

<151> 2003-07-21

<160> 4

<170> PatentIn version 3.3

<210> 1

<211> 1325

<212> DNA

<213> Escherichia coli

<220>

<221> CDS

<222> (1)..(954)

<400> 1

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Met Met Lys Cys Ile Leu Leu Lys Trp Ile Leu Cys Leu Leu Leu Gly	
1 5 10 15	
ttt tct tcg gta tcc tat tcc cag gag ttt acg ata gac ttt tcg act	96
Phe Ser Ser Val Ser Tyr Ser Gln Glu Phe Thr Ile Asp Phe Ser Thr	
20 25 30	
caa caa agt tat gta tct tcg tta aat agt ata cgg aca gtg ata tcg	144
Gln Gln Ser Tyr Val Ser Ser Leu Asn Ser Ile Arg Thr Val Ile Ser	
35 40 45	
acc cct ctt gaa cat ata tct cag gga gct aca tcg gta tcc gtt att	192
Thr Pro Leu Glu His Ile Ser Gln Gly Ala Thr Ser Val Ser Val Ile	
50 55 60	
aat cat aca cca cca gga agt tat att tcc gta ggt ata cga ggg ctt	240
Asn His Thr Pro Pro Gly Ser Tyr Ile Ser Val Gly Ile Arg Gly Leu	
65 70 75 80	
gat gtt tat cag gag cgt ttt gac cat ctt cgt ctg att att gaa cga	288
Asp Val Tyr Gln Glu Arg Phe Asp His Leu Arg Leu Ile Ile Glu Arg	
85 90 95	
aat aat tta tat gtg gct gga ttt gtt aat acg aca aca aat act ttc	336
Asn Asn Leu Tyr Val Ala Gly Phe Val Asn Thr Thr Thr Asn Thr Phe	
100 105 110	
tac aga ttt tca gat ttt gca cat ata tca ttg ccc ggt gtg aca act	384
Tyr Arg Phe Ser Asp Phe Ala His Ile Ser Leu Pro Gly Val Thr Thr	
115 120 125	
att tcc atg aca acg gac agc agt tat acc act ctg caa cgt gtc gca	432

Substitute Sequence Listing

Ile	Ser	Met	Thr	Thr	Asp	Ser	Ser	Tyr	Thr	Thr	Leu	Gln	Arg	Val	Ala	
130						135					140					
gcg	ctg	gaa	cgt	tcc	gga	atg	caa	atc	agt	cgt	cac	tca	ctg	gtt	tca	480
Ala	Leu	Glu	Arg	Ser	Gly	Met	Gln	Ile	Ser	Arg	His	Ser	Leu	Val	Ser	
145					150					155					160	
tca	tat	ctg	gcg	tta	atg	gag	ttc	agt	ggt	aat	aca	atg	acc	aga	gat	528
Ser	Tyr	Leu	Ala	Leu	Met	Glu	Phe	Ser	Gly	Asn	Thr	Met	Thr	Arg	Asp	
				165					170					175		
gca	tca	aga	gca	gtt	ctg	cgt	ttt	gtc	act	gtc	aca	gca	gaa	gcc	tta	576
Ala	Ser	Arg	Ala	Val	Leu	Arg	Phe	Val	Thr	Val	Thr	Ala	Glu	Ala	Leu	
			180					185					190			
cgg	ttc	agg	caa	ata	cag	aga	gaa	ttt	cgt	ctg	gca	ctg	tct	gaa	act	624
Arg	Phe	Arg	Gln	Ile	Gln	Arg	Glu	Phe	Arg	Leu	Ala	Leu	Ser	Glu	Thr	
		195					200					205				
gct	cct	gtt	tat	acg	atg	acg	ccg	gaa	gac	gtg	gac	ctc	act	ctg	aac	672
Ala	Pro	Val	Tyr	Thr	Met	Thr	Pro	Glu	Asp	Val	Asp	Leu	Thr	Leu	Asn	
	210					215					220					
tgg	ggg	aga	atc	agc	aat	gtg	ctt	ccg	gag	tat	cgg	gga	gag	gct	ggt	720
Trp	Gly	Arg	Ile	Ser	Asn	Val	Leu	Pro	Glu	Tyr	Arg	Gly	Glu	Ala	Gly	
225					230					235					240	
gtc	aga	gtg	ggg	aga	ata	tcc	ttt	aat	aat	ata	tca	gcg	ata	ctt	ggt	768
Val	Arg	Val	Gly	Arg	Ile	Ser	Phe	Asn	Asn	Ile	Ser	Ala	Ile	Leu	Gly	
				245					250					255		
act	gtg	gcc	gtt	ata	ctg	aat	tgt	gga	aat	tca	tca	aga	aca	atc	aca	816
Thr	Val	Ala	Val	Ile	Leu	Asn	Cys	Gly	Asn	Ser	Ser	Arg	Thr	Ile	Thr	
			260					265					270			
ggt	gat	act	tgt	aat	gag	gag	acc	cag	aat	ctg	agc	aca	ata	tat	ctc	864
Gly	Asp	Thr	Cys	Asn	Glu	Glu	Thr	Gln	Asn	Leu	Ser	Thr	Ile	Tyr	Leu	
		275					280					285				
agg	gaa	tat	caa	tca	aaa	gtt	aag	agg	cag	ata	ttt	tca	gac	tat	cag	912
Arg	Glu	Tyr	Gln	Ser	Lys	Val	Lys	Arg	Gln	Ile	Phe	Ser	Asp	Tyr	Gln	
	290					295					300					
tca	gag	gtt	gac	ata	tat	aac	aga	att	cgg	gat	gaa	tta	tga			954
Ser	Glu	Val	Asp	Ile	Tyr	Asn	Arg	Ile	Arg	Asp	Glu	Leu				
305					310					315						
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ctccccagac	tattacagaa	ctatgttcgg	aatatcgcaa	cacacaaata	tatacgataa											1074
atgacaagat	actatcatat	acggaatcga	tggcaggcaa	aagagaaatg	gttatcatta											1134
catttaagag	cggcgaaaca	tttcaggtcg	aagtcccggg	cagtcaacat	atagactccc											1194
agaaaaaagc	cattgaaagg	atgaaggaca	cattaagaat	cacatatctg	accgagacca											1254
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tgaaaaacta	g															1325

Substitute Sequence Listing

<211> 317

<212> PRT

<213> Escherichia coli

<400> 2

Met Met Lys Cys Ile Leu Leu Lys Trp Ile Leu Cys Leu Leu Leu Gly
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Phe Ser Ser Val Ser Tyr Ser Gln Glu Phe Thr Ile Asp Phe Ser Thr
20 25 30

Gln Gln Ser Tyr Val Ser Ser Leu Asn Ser Ile Arg Thr Val Ile Ser
35 40 45

Thr Pro Leu Glu His Ile Ser Gln Gly Ala Thr Ser Val Ser Val Ile
50 55 60

Asn His Thr Pro Pro Gly Ser Tyr Ile Ser Val Gly Ile Arg Gly Leu
65 70 75 80

Asp Val Tyr Gln Glu Arg Phe Asp His Leu Arg Leu Ile Ile Glu Arg
85 90 95

Asn Asn Leu Tyr Val Ala Gly Phe Val Asn Thr Thr Thr Asn Thr Phe
100 105 110

Tyr Arg Phe Ser Asp Phe Ala His Ile Ser Leu Pro Gly Val Thr Thr
115 120 125

Ile Ser Met Thr Thr Asp Ser Ser Tyr Thr Thr Leu Gln Arg Val Ala
130 135 140

Ala Leu Glu Arg Ser Gly Met Gln Ile Ser Arg His Ser Leu Val Ser
145 150 155 160

Ser Tyr Leu Ala Leu Met Glu Phe Ser Gly Asn Thr Met Thr Arg Asp
165 170 175

Ala Ser Arg Ala Val Leu Arg Phe Val Thr Val Thr Ala Glu Ala Leu
180 185 190

Arg Phe Arg Gln Ile Gln Arg Glu Phe Arg Leu Ala Leu Ser Glu Thr
195 200 205

Ala Pro Val Tyr Thr Met Thr Pro Glu Asp Val Asp Leu Thr Leu Asn
210 215 220

Trp Gly Arg Ile Ser Asn Val Leu Pro Glu Tyr Arg Gly Glu Ala Gly
225 230 235 240 245 250

Substitute Sequence Listing

225 230 235 240

Val Arg Val Gly Arg Ile Ser Phe Asn Asn Ile Ser Ala Ile Leu Gly
245 250 255

Thr Val Ala Val Ile Leu Asn Cys Gly Asn Ser Ser Arg Thr Ile Thr
260 265 270

Gly Asp Thr Cys Asn Glu Glu Thr Gln Asn Leu Ser Thr Ile Tyr Leu
275 280 285

Arg Glu Tyr Gln Ser Lys Val Lys Arg Gln Ile Phe Ser Asp Tyr Gln
290 295 300

Ser Glu Val Asp Ile Tyr Asn Arg Ile Arg Asp Glu Leu
305 310 315

<210> 3
<211> 1325
<212> DNA
<213> Escherichia coli

<220>
<221> CDS
<222> (951)..(1322)

<400> 3
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aatagtatac ggacagtgat atcgaccctt cttgaacata tatctcaggg agctacatcg 180
gtatccgtta ttaatcatac accaccagga agttatattt ccgtaggtat acgagggcgtt 240
gatgtttatc aggagcgttt tgaccatctt cgtctgatta ttgaacgaaa taatttatat 300
gtggctggat ttgttaatac gacaacaaat actttctaca gattttcaga ttttgcatat 360
atatcattgc ccggtgtgac aactatttcc atgacaacgg acagcagtta taccactctg 420
caacgtgtcg cagcgtgga acgttccgga atgcaaata gtcgtcactc actgggttca 480
tcatatctgg cgtaaatgga gttcagtgg aatacaatga ccagagatgc atcaagagca 540
gttctgcgtt ttgtcactgt cacagcagaa gccttacggt tcaggcaaat acagagagaa 600
tttcgtctgg cactgtctga aactgctcct gtttatacga tgacgccgga agacgtggac 660
ctcactctga actgggggag aatcagcaat gtgcttccgg agtatcgggg agaggctggt 720
gtcagagtgg ggagaatatc ctttaataat atatcagcga tacttggtac tgtggccggt 780
atactgaatt gtggaaattc atcaagaaca atcacaggtg atacttgtaa tgaggagacc 840
cagaatctga gcacaatata tctcagggaa tatcaatcaa aagttaagag gcagatattt 900

Substitute Sequence Listing

tcagactatc agtcagaggt tgacatatat aacagaattc gggatgaatt atg aat	956
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aaa gta aaa tgt tat gtt tta ttt acg gcg tta cta tcc tct cta tat	1004
Lys Val Lys Cys Tyr Val Leu Phe Thr Ala Leu Leu Ser Ser Leu Tyr	
5 10 15	
gca cac gga gct ccc cag act att aca gaa cta tgt tcg gaa tat cgc	1052
Ala His Gly Ala Pro Gln Thr Ile Thr Glu Leu Cys Ser Glu Tyr Arg	
20 25 30	
aac aca caa ata tat acg ata aat gac aag ata cta tca tat acg gaa	1100
Asn Thr Gln Ile Tyr Thr Ile Asn Asp Lys Ile Leu Ser Tyr Thr Glu	
35 40 45 50	
tcg atg gca ggc aaa aga gaa atg gtt atc att aca ttt aag agc ggc	1148
Ser Met Ala Gly Lys Arg Glu Met Val Ile Ile Thr Phe Lys Ser Gly	
55 60 65	
gaa aca ttt cag gtc gaa gtc ccg ggc agt caa cat ata gac tcc cag	1196
Glu Thr Phe Gln Val Glu Val Pro Gly Ser Gln His Ile Asp Ser Gln	
70 75 80	
aaa aaa gcc att gaa agg atg aag gac aca tta aga atc aca tat ctg	1244
Lys Lys Ala Ile Glu Arg Met Lys Asp Thr Leu Arg Ile Thr Tyr Leu	
85 90 95	
acc gag acc aaa att gat aaa tta tgt gta tgg aat aat aaa acc ccc	1292
Thr Glu Thr Lys Ile Asp Lys Leu Cys Val Trp Asn Asn Lys Thr Pro	
100 105 110	
aat tca att gcg gca atc agt atg aaa aac tag	1325
Asn Ser Ile Ala Ala Ile Ser Met Lys Asn	
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<210> 4
 <211> 124
 <212> PRT
 <213> Escherichia coli
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Met Asn Lys Val Lys Cys Tyr Val Leu Phe Thr Ala Leu Leu Ser Ser
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Leu Tyr Ala His Gly Ala Pro Gln Thr Ile Thr Glu Leu Cys Ser Glu
20 25 30
Tyr Arg Asn Thr Gln Ile Tyr Thr Ile Asn Asp Lys Ile Leu Ser Tyr
35 40 45
Thr Glu Ser Met Ala Gly Lys Arg Glu Met Val Ile Ile Thr Phe Lys
50 55 60
Ser Gly Glu Thr Phe Gln Val Glu Val Pro Gly Ser Gln His Ile Asp
65 70 75 80

Substitute Sequence Listing

Ser Gln Lys Lys Ala Ile Glu Arg Met Lys Asp Thr Leu Arg Ile Thr
85 90 95

Tyr Leu Thr Glu Thr Lys Ile Asp Lys Leu Cys Val Trp Asn Asn Lys
100 105 110

Thr Pro Asn Ser Ile Ala Ala Ile Ser Met Lys Asn
115 120